REMARKS

Claims 1-17 remain pending in the application. Claims 7 and 8 have been amended.

Claims 1-4, and 9 stand rejected under 35 U.S.C. § 112, first paragraph, as, the specification, while allegedly being enabling for the specific compounds of claims 5-8, allegedly does not reasonably provide enablement for the entire scope of the phrases "NK1 receptor antagonists" or "GABA analogs." It is further stated in the Office Action that the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate with the scope of the present claims.

Applicants submit herewith two literature references describing assays for determining the activity of NK1 antagonist and alpha-2-ligands. The references to Boyle, et al. and Gee, et al. provide examples of assays for determining the activity of NK1 antagonist and alpha-2-delta ligands, respectively.

In addition to the examples of compounds which act as NK1 antagonist and GABA analogs provided in the present specification, one of ordinary skill in the art would have been aware of the literature test methods for identifying such compounds. The enclosed references were available to the public as of the priority date of the present invention and, therefore, one of ordinary skill in the art would readily have been able to identify other NK1 antagonist and GABA analogs (gabapentin and pregabalin, which are referred to as GABA analogs in the application, were known to have alpha-2-delta activity) in addition to the compounds specifically exemplified in the application. It is respectfully submitted that the functional definition used in the claims is clear, supported by the description, and is a reasonable representation of the contribution made to the art by the present invention. Accordingly, Applicants respectfully submit that they are entitled to a breadth of protection commensurate with the contribution made to the art by the invention and thus, that the scope present claims are sufficiently enabled. Accordingly, for the above-reasons Applicants respectfully submit that claims 1-4 and 9 satisfy 35 U.S.C. § 112, first paragraph and applicants request that the Examiner remove the rejection on this ground.

Claims 1-18 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Horwell, et al. and Bryans, et al. Reconsideration of the rejection under 35 U.S.C. § 103(a) is as unpatentable over Horwell, et al. in view Bryans, et al. is respectfully requested.

In the Office Action it is stated that Horwell, et al. teach that NK1 receptor antagonist compounds are used for treating pain and Bryans, et al. teach that GABA analogs compounds are also useful for treating pain. As stated in the previous Amendment and Response, the claims of the present application are direct to a method for treating chronic pain comprising administering to a patient in need of treatment an effective amount of a synergistic combination of a NK1 receptor antagonist and GABA analog. In the present Office Action, it stated that "the instant Figures 2(b) and 2 (c) set forth that there is a general expectation in the art to observe and improved chronic pain control by adding gabapentin and NK1 antagonist". Applicants respectfully disagree. Applicants submit that one of ordinary skill in the art, aware that NK1 antagonist and gabapentin both had utility in the treatment of pain, would at best expect to see an additive effect by using the agents in combination. However, Applicants have unexpectedly found that the claimed combination gives a greater than additive, that is a synergistic, effect. This can clearly be seen from the Figures presented in the description, which provide a comparison of the calculated additive effect in the observed greater, synergistic effect. Such an effect could not have been predicted and one of ordinary skill in the art, aware of the prior art, could not have been motivated to test the combination with a reasonable expectation of success (i.e. of achieving synergy). The observation of synergy is, in itself, an unexpected result. Thus, Applicants respectfully submit that the presently pending claims are not obvious in light of the cited art.

It is further stated in the Office Action that the "presented results are directed to specific dosing, specific compounds, and specific regimens. The presented claims are not commensurate with the scope of such data". Applicants respectfully disagree. The data presented relates to different NK1 antagonists and several different dose ratios. Gabapentin is the best-known GABA analog, and it is credible that the effects observed for gabapentin would also be observed for other GABA analogs, such as pregabalin, which have the same mechanism of action. The technical teaching provided by the

invention is that the combination of a compound with NK1 antagonist activity and a GABA analog provides a greater than expected improvement in the treatment of chronic pain. Accordingly, Applicants respectfully submit that the scope of the present claims is commensurate with the contribution to the art provided by the invention and that the present claims are a reasonable extrapolation of the examples provided in the specification.

Accordingly, Applicants respectfully submit that the supra-additive effect is unexpected and surprising and that Applicants have provided an advance and potential pain therapies. Accordingly, Applicants respectfully submit that the data provided in the application demonstrates that the presently claimed in invention is non-obvious in light of both Horwell, et al. and Bryans, et al. None of the references, either individually or in combination teach the claimed synergy. Reconsideration is respectfully requested.

In view of the present amendment and foregoing remarks, reconsideration of the rejection and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with the communication to our deposit account number 23-0455.

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Respectfully submitted,

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Attachments: Boyle et al., Bioorganic & Medicinal Chemistry, 2(5), 357-370, 1994
Gee et al., J. Biological Chemistry, 271(10), 5768-5776, 1996